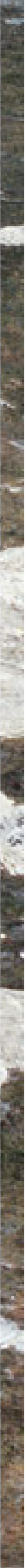

PHOTOS COURTESY OF MARI HOLLINGSWORTH AND DOUG MASSEY

# Pathogen Risks *From* Applying Sewage Sludge to Land

Despite complaints of related illnesses, little is known about the dangers of spreading biosolids on land.

DAVID L. LEWIS AND DAVID K. GATTIE

In the late 1980s, the U.S. Congress banned ocean dumping of municipal wastes. As an alternative, the EPA promulgated in 1993 what has become known as the 503 Rule (40 CFR Part 503), which allows and regulates land application of processed sewage sludges, or biosolids (*1*). Currently, the United States and a growing number of Western European countries apply approximately half of their sewage sludge onto land, mainly for agricultural purposes (*2*). Public health and environmental concerns about land application of biosolids have historically centered on the presence of heavy metals, pesticides, PCBs, and other chemical contaminants. Now, amid increasing complaints about illnesses and even deaths of several residents who lived near land application sites, a debate rages over whether risks from pathogens in sludge should be of greater concern.

Reports of illnesses and deaths from residents living near land application sites who are exposed to dust and water runoff from fields treated with sewage sludges indicate a pattern of chemical irritation. Symptoms, such as burning eyes, burning lungs, difficulty in breathing, and skin rashes, are followed within days to months by complaints of gastrointestinal, skin, and respiratory infections (*3*). The photo on page 290A is an example of a skin-related infection. However, a lack of risk assessments performed before or since the 503 Rule's implementation regarding public exposure to bacteria, viruses, and other disease-causing microorganisms found in most sludges hampers our ability to evaluate such complaints (*4*). Rule 503 was promulgated without pathogen risk assessment. Therefore, there is little known about the risks of pathogen exposure from sludge permitted under Rule 503.

Others dismiss reports of illness as purely anecdotal. They argue that the only problem is public perception and point to a lack of documented cases in the medical literature as proof that land applications of biosolids are well managed and safe. Those who believe that they have been harmed respond that adverse effects are not monitored and proper epidemiological studies have never been undertaken.

Unfortunately, both sides are arguing over science that has not been done. Thus, it is not a dispute over interpretation of data, but over how to interpret a lack of data. In addition, EPA has relatively little expertise in infection control and no system or plan for monitoring infectious diseases nationwide. Yet, the agency has the responsibility of overseeing, processing, and disposing of what is probably the nation's largest repository of potentially infectious human material.

Two years ago, EPA asked the National Academy of Sciences to review the science and methodology behind the 503 Rule and invited assistance from the National Institute of Occupational Safety & Health (NIOSH), which is an arm of the Centers for Disease Control and Prevention (CDC). EPA has placed a high priority on addressing the National Academy of Sciences' recommendations, which are due out this spring. Meanwhile, NIOSH has published infection control guidelines for workers handling the most common type of biosolid (*5*). A properly managed biosolids program that merges the expertise of the CDC with the regulatory authority of EPA may be the best way to ensure that public health and the environment are adequately protected in this case. This feature looks at the questions about infectious disease risks being raised regarding applying biosolids to land.

## A healthy debate

The 503 Rule permits two classes of biosolids for agricultural use: Class A and Class B. Class A sludges are materials that are considered safe for immediate and direct contact with humans and animals on the basis of various microbiological assays and process requirements intended to ensure that pathogens are below the detection limits. No crop restrictions are placed on sites treated with Class A sewage sludges.


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**At fields treated with Class B biosolids, EPA recommends posting signs or erecting fences to restrict public access for 30 days or longer.**

Class B sludges, which account for most land-applied biosolids, have been treated to reduce pathogen levels using various waste treatment processes, such as anaerobic digestion and pH elevation (lime stabilization). They are required to meet certain maximum pathogen levels; for example, average fecal coliform levels must be below 2 million colony-forming units of bacteria per gram of dry sludge. EPA stipulates that depending on various land uses, public access to Class B land application sites be restricted for up to one year to allow natural attenuation of pathogen levels.

Typically, a rule such as the 503 Rule is reviewed by EPA's Office of Research and Development (ORD) for scientific credibility. Changes or additional research are recommended by ORD, while the various program offices involved in drafting, reviewing, and modifying rules approve the language of the proposed rules.

The 503 Rule was a notable exception. ORD scientists argued that protection of the public health and environment from chemical pollutants and pathogens in sewage sludges could not be fully assured. Nevertheless, under a court order to develop a guidance document for land application, federal rules for land application moved forward without broad support from ORD scientists. In a similar case, the use of methyl *tert*-butyl ether (MTBE) as a fuel additive was approved despite ORD scientists arguing that the additive would become a serious drinking water contaminant (*6*). Although MTBE and sewage sludges involve very different areas of risk assessment, they both emphasize an increasingly clear lesson for policy makers—rules based on inadequate science are likely to create rather than solve environmental and public health problems.

In the case of the 503 Rule, the ORD took the unprecedented step of refusing to concur unless a preamble was published with the rule acknowledging its scientific uncertainties. ORD's scientists recommended undertaking the comprehensive research program outlined in the preamble (*1*). However, the Office of Water has placed a low priority on funding biosolids research, and EPA met very little of its original $10 million commitment to address uncertainties.

Although the ecological effects of pathogens were addressed in the preamble, EPA could not have anticipated the current turmoil over human illnesses. EPA's mission includes protecting the public from biological threats; however, it has historically concentrated its efforts on chemical and engineering problems (*7*). Even most microbiologists working for ORD have focused on issues involving biodegradation of chemical pollutants rather than risks that microorganisms pose to public health.

Recent reports by EPA's Office of the Inspector General (OIG) concluded that EPA does not effectively ensure compliance with the 503 Rule (*8, 9*). Regarding the research needs identified in the preamble, OIG concluded, "There are no plans to complete the comprehensive study, and uncertainties remain unaddressed by further research."

In 1996, the National Research Council (NRC) reviewed the Rule 503 standards and the effectiveness of waste treatment processes (*4*). NRC recognized that little information existed on risks of infection from land-applied sewage sludges, no formal risk assessment for pathogens had ever been done, regrowth of pathogens may occur after waste treatment, and infections from exposure to sewage sludges may go unreported. In their report, NRC urged EPA to develop effective ways to monitor specific pathogens and asked that the agency reevaluate the adequacy of their 30-day waiting period for grazing animals to stay off land treated with biosolids. EPA, so far, has not developed a means for monitoring specific pathogens or changed its approach to dealing with pathogen risks.

## Pathogens in sewage sludges

EPA and others have compiled lists of various pathogenic bacteria, viruses, protozoa, and parasitic worms potentially found in sewage sludges (Table 1). Such lists focus on enteric organisms historically associated with wastewater problems and need updating to include other potentially important pathogens and emerging infectious diseases. Municipal wastes from any large metropolitan area are likely to include a wide variety of pathogens from every corner of the world.

For example, cytomegalovirus (CMV) specifically infects humans and is found in 60–90% of the adult population in the United States. (*10*). The virus is shed in excrement for months to years after infection. Exposure during pregnancy is a leading cause of certain birth defects, such as vision and hearing impairments and mental retardation. Fifty percent of young women in the higher socioeconomic brackets (individuals who tend to live under good sanitary conditions and therefore are not infected earlier) in the United States are susceptible to CMV infection (*11*). Similarly, human papiloma virus (HPV), the fastest growing sexually transmitted disease in the United States, is the primary cause of cervical cancer and a significant risk factor for colorectal cancer. HPV is environmentally stable and may have become a ubiquitous contaminant in municipal wastes in recent years. Abattoirs and funeral homes introduce large numbers of nonenteric pathogens into waste treatment systems, including a wide variety of common bloodborne pathogens and rare but extremely stable prions, which are the probable causes of Creutzfeldt–Jakob and Mad Cow diseases.

The public health implications of these sources of infectious agents need to be fully assessed with respect to land application practices. Processed sewage sludges often contain the combined wastes from many hundreds of thousands of individuals, and most waste treatment processes are not designed to sterilize the material. It is prudent, therefore, to assume that any organism commonly found in municipal wastes is also likely to be present in Class B biosolids.

TABLE 1

### Class B contents

The following organisms are examples of pathogens found in Class B sewage sludge and associated symptoms of exposure. One or more species from the following groups of genera may be represented in Class B sludge.

| Bacteria | | Symptoms |
|---|---|---|
| *Aeromonas* | *Legionella* | Fever, chills, nausea, vomiting, severe abdominal pain, diarrhea, bloody stools, respiratory and sinus congestion, thick/colored mucus, rashes |
| *Bacillus* | *Listeria* | |
| *Brucella* | *Mycobacterium* | |
| *Campylobacter* | *Proteus* | |
| *Citrobacter* | *Pseudomonas* | |
| *Clostridium* | *Salmonella* | |
| *Coxiella* | *Shigella* | |
| *Enterobacter* | *Serratia* | |
| *Erysipelothrix* | *Staphylococcus* | |
| *Escherichia* | *Streptococcus* | |
| *Francisella* | *Yersinia* | |
| *Klebsiella* | *Vibrio* | |
| **Viruses** | | |
| Astroviruses | Norwalk viruses | Fever, chills, nausea, vomiting, abdominal pain, diarrhea, severe headaches, congestion, respiratory distress, jaundice, paralysis, rashes |
| Caliciviruses | Reoviruses | |
| Hepatitis viruses | Rotaviruses | |
| Enteroviruses | | |
| **Protozoa** | | |
| *Balantidium* | *Giardia* | Intermittent diarrhea/constipation, abdominal pain/cramps, bloody stools, nausea, weight loss, dehydration |
| *Cryptosporidium* | *Toxoplasma* | |
| *Entamoeba* | | |
| **Helminth Worms** | | |
| *Ascaris* | *Taenia* | Fever, chest pain, bronchitis, diarrhea, vomiting, nutritional deficiencies, neurological problems, anorexia, weight loss, muscle aches |
| *Hymenolepis* | *Trichuris* | |
| *Necator* | *Toxocara* | |

**Source:** U.S. EPA Office of Research and Development.

## What are the risks?

***Minimum infective dose.*** A complex set of conditions determines whether someone will develop an infection or a disease from exposure to sewage sludge pathogens. To begin with, exposure to pathogens may only lead to "pseudo-infections" in which pathogens have been introduced in the body but fail to cause disease. In other cases, pathogens take hold, multiply, and, in time, cause disease.

Infectious diseases develop when susceptible individuals are exposed to enough virulent, infectious units, such as bacterial cells or viral particles, through an appropriate mechanism of entry—for example, by inhalation, ingestion, or dermal contact. Host susceptibility, exposure, dose, virulence, and portal of entry are the primary limiting factors in the disease process.

EPA is currently considering assessing pathogen risks with sludges based on estimates of minimum infective doses (MIDs). Reliable estimates of the MID, minimum number of infectious units required to cause an infection, are elusive. These numbers are based on data from individuals with normal immune systems and vary widely, both spatially and temporally. With immunocompromised individuals, such as infants, the elderly, or those with AIDS and other chronic diseases, what constitutes the MID is unknown.

***Pathogen–chemical risks.*** Although the subject of biosolids is often introduced with a discussion of night soil (human excrement used for fertilizer) the current practice of concentrating urban and industrial wastes with excrement from the global community bears little resemblance to farm life in the "old world." To process sewage into Class B biosolids, the material is partially disinfected by heat, chemicals, or biological processes. These methods can release large amounts of endotoxins from the breakdown of cell walls of gram-negative bacteria, which are the kind of bacteria that comprise most of the living biomass in sewage sludges. When ingested or inhaled, endotoxins interfere with the body's natural defense mechanisms. Lime and cationic dewatering polymers, which can enhance the irritant properties of the mixture, may also be added during wastewater and sludge treatment. Sewage sludge also contains household products, industrial wastes, and other chemicals that may compromise the body's defenses against infection by irritating the skin, eyes, and respiratory and gastrointestinal tracts (*12–14*).

Several tons or more per acre of the final product are distributed annually for land application in populated areas. Once applied, the material can form organic dusts as it dries, further concentrating pathogens and irritant chemicals. Sewage sludge may also enhance the toxicity of some agricultural chemicals, adding yet another variable to complex pathogen–chemical interactions at land application sites (*15*).

TINA CHILDERS

**A surgical wound on the thigh of a 34-year-old male in Menifee, Calif., became infected with *Staphylococcus epidermitis*, which developed after the undressed wound was exposed to soil blowing from a field treated with Class B biosolids.**

Degradation of the biological and chemical components of sludge in the field can produce various volatile irritants, including inorganic and organic sulfides, volatile fatty acids, alkyl amines, and ammonia. Emissions of these compounds may cause eye and mucus membrane irritation and respiratory problems, thus affecting host susceptibility (*13*). Although pathogens die off following application, winds may carry dusts embedded with viable pathogens and irritant chemicals for miles (*16*).

The bottom line is that land application of Class B sewage sludges is not a simple issue of pathogen versus chemical contaminant risks. The material contains pathogens and mixtures of chemicals that can facilitate the infection process. This presents a pathogen–chemical risk—something about which we know very little.

In our own study, we found that 25% of 48 individuals living near land application sites who complained of chemical irritation had evidence of serious *Staphylococcus aureus* infections, which contributed to two deaths (*3*). *S. aureus* tends to invade damaged tissues and is a common complication of diaper rash, in which feces and urine irritate the skin (*17, 18*). These observations suggest that irritant chemicals may elevate risks of infection from low levels of pathogens in sewage sludges, especially with organisms such as staphylococci that tend to enter the body through irritated mucus membranes and skin abrasions.

What are the chances that applying millions of tons of organic matter embedded with irritant chemicals and pathogens nationwide will create a new and significant environmental source of infectious diseases? This prospect merits the performance of comprehensive risk assessments by infectious disease experts and microbial ecologists.

## Epidemiological studies

Retrospective studies of infections among workers handling processed sewage sludge have indicated potential problems with enteric pathogens and endotoxins in air and sludge samples (*5, 19*). However, the only published prospective epidemiological study, which investigated farm families in Ohio, found no elevated risks of infection (*20*). The authors did not report the levels of pathogens in the sludges, and they cautioned against extrapolating their results to other sites because of the low application rates used (an average of 2–10 dry metric tons/ha/yr). In short, almost no reliable epidemiological data exist.

Because we are dealing with complex pathogen–chemical risks, infections are likely to vary qualitatively and quantitatively. For example, the numbers and kinds of infections will depend on the particular combination of chemicals and pathogens, the batch of sludge, and environmental conditions. This makes prospective epidemiological studies inherently likely to overlook problems. Retrospective studies of sites reporting problems, on the other hand, are more likely to reveal the nature and scope of risks. However, this requires developing a comprehensive system for monitoring communities surrounding land application sites.

Some experts argue that this is not worthwhile, because if significant numbers of infections were occurring, there would be documentation of them by public health officials. Moreover, workers should have the highest exposure levels, but their infection rates are low. Others counter that some studies of wastewater workers have indicated elevated risks of infection (*21–23*). Also, low rates of reported infections may only reflect that workers comprise a generally healthy group compared with the general population, which includes individuals more vulnerable to infection. It has also been pointed out that the primary route of infection for workers—hand-to-mouth ingestion—is different than inhaling dusts from fields on which pathogens and irritant chemicals have concentrated after drying. In other words, we cannot compare apples with oranges.

These same arguments have played out in settings involving state and federal guidelines for infection control and may provide guidance in the current debate. In 1990, for example, virtually all dentists in the United States disinfected only the outside of handpieces used to drill and clean teeth. That changed after six patients in Florida unknowingly contracted HIV in a dental practice run by an HIV-infected dentist. It was found that HIV and other infectious agents embedded in blood-contaminated lubricants expelled by equipment for cleaning and drilling teeth can escape disinfection and remain highly infectious for days (*24, 25*). Patient-to-patient transmissions from contaminated equipment can potentially be a greater risk than accidental needlestick injuries among healthcare workers (*26*). As a result, the CDC published new heat-sterilization recommendations for dentistry (*27*).

More recently, officials underestimated the risk of anthrax spores dispersed through the mail. On the basis of indications that the MID is tens of thousands of spores, risks from handling contaminated letters were at first considered infinitesimal. However, DNA analyses confirmed that more than a dozen people were infected from handling letters cross-contaminated at a mail distribution center (*29*). Government officials were then compelled to irradiate the mail and decontaminate buildings.

So far, no one has applied DNA fingerprinting techniques to see if infections can be traced to sewage sludges. Without such ironclad proof, infections associated with exposures to sewage sludges are likely to be considered anecdotal. Unfortunately, committing high-tech resources to pinpointing sources of infections normally occurs only after a large outbreak or the transmission of some organism of particular concern to public health, such as *E. coli*, HIV, anthrax, or tuberculosis. Sporadic infections scattered among the general population involving most of the kinds of pathogens found in sewage sludges are unlikely to ever attract the resources it would take to determine their sources. Nevertheless, considering that potentially millions of individuals in the United States may be unwittingly exposed to pathogens in Class B biosolids, total numbers of undocumented cases could be quite high.

## Filling gaps with mathematical models

Without reliable risk assessments and a monitoring system in place, predictive mathematical models are sometimes used to fill gaps in empirical data. Despite being grounded in impressively complex mathematical relationships, modeling results are highly biased by the input data and parameter assumptions. Therefore, results can often be misleading and unreliable.

Pasquill's classical model describes transport of airborne particulates emitted from a point source such as stockpiled sewage sludges (*29*). To estimate risks of infection, Lighthart and Frisch modified this model to account for inactivation of microbial populations from desiccation and exposure to solar UV radiation (*30*). Expanding this approach, Parker and co-workers described the transport of microbial aerosols from an area source, such as a tract of treated land (*31*).

To assess human health risks from airborne contaminants, these aerosol transport models are used to predict concentrations of viable microorganisms at various distances from a source. To generate these risk assessments, concentration outputs are integrated with dose–response data from human ingestion studies of enteric organisms. Pillai et al. predicted that a population center 6 km from a land application site in western Texas was not impacted by airborne bacterial pathogens (*32*). On the other hand, Dowd et al. predicted that a high risk of infection could exist under certain conditions for populations near land application sites (*16*). For example, they estimated a 94% risk of viral infection under moderate wind conditions 100 m from a site during sludge application.

Current models neglect important biological and ecological factors, causing them to underestimate risks. Pathogens in sewage sludges, by and large, are embedded in aggregates of organic matter. Because of this, they are extremely resistant to environmental effects, which form the basis for model inactivation rates (*33, 34*). UV light, for example, only affects microorganisms on the outer exposed surfaces of soil aggregates. Even then, bacteria may recover by photoreactivation, a process whereby UV-damaged DNA is enzymatically repaired after cells are exposed to visible or near-visible light (*36*). Cells embedded in aggregates, especially those containing lipid and protein matter, require special isolation techniques for enumeration and are highly resistant to disinfection (*26*).

To estimate bacterial survival rates, models often rely on data from experiments with enteric microorganisms, such as *E. coli* and *Salmonella*. These organisms are short-lived compared with organisms that form spores or are encapsulated, such as *Mycobacterium* species. Moreover, the models assume that exposed individuals have normal immune systems, and they fail to recognize that exposures to endotoxins and other components of sewage sludges could render healthy individuals prone to infection.

In addition to underestimating risks based on these factors, modeling natural microbial processes is inherently fraught with very large degrees of error (*36*). Consequently, when using models to estimate relative exposure levels to airborne sludge contaminants, we chose not to rely on biological emission rates but rather on subroutines based on well-understood physical processes dealing with air dispersion (*3*).

The 1996 NRC report also found risk assessment models unreliable, concluding, "Presently, it would be premature to give too much weight to the results of any of the existing models" (*4*). Mathematical models, at least for the foreseeable future, will be quite useful in assessing the physical transport of microorganisms but apt to be very misleading for predicting infection risks.

## Managing pathogen risks

***Focusing on exposure and entry.*** Of the primary factors that limit risks of infection, NIOSH decided to focus on portal of entry. For example, workers handling Class B biosolids are primarily infected hand-to-mouth if they fail to wear gloves or wash their hands before eating. Therefore, NIOSH recommended standard hygienic measures, including frequent hand-washing and wearing gloves and masks while working with the material (*5*).

Public exposure, on the other hand, occurs primarily after pathogens from Class B biosolids are transported by air or water away from land application sites. Microorganisms in dusts from treated fields may be directly inhaled or swallowed, ingested hand-to-mouth, or, to a lesser extent, introduced through drinking water or food obtained near the application site.

Public concerns associated with sewage sludges may not be resolved simply by banning Class B sludges.

Limiting exposure to windblown dusts and water runoff would diminish the general population's risk of infection from pathogens in Class B biosolids. However, EPA has concluded that properly treated biosolids present no significant risk of infection and therefore does not restrict or monitor land application in areas where residential communities are close to land application sites and in the direct path of dusts blowing from treated fields.

This may be an area in which the safety of land application practices could be improved if current standards are deemed inadequately protective. Current transport models can guide land application operators in selecting sites that would minimize exposure to surrounding communities. Standards could also be developed that reduce the levels of pathogenic dusts and volatile emissions.

***Applying the pathogen–chemical risk paradigm.*** Host susceptibility is a primary factor to consider when evaluating infection risks. Exposures to chemicals that break down barriers to infection effectively lower the numbers of organisms required to cause an infection. MID probably has little meaning when pathogens are combined with chemicals that markedly enhance the infection process. Whenever possible, steps should be taken to reduce the levels of chemicals in sewage sludge that cause skin rashes, bronchial congestion, colitis, and other symptoms that can increase susceptibility to infection. The focus of attention should be on such components as nickel salts and endotoxins, which can be highly irritating to skin, mucus membranes, and the respiratory and gastrointestinal tracts, especially in sensitive populations.

Heavy congestion, a symptom frequently reported among people potentially exposed to sewage sludge dusts, is part of the respiratory system's inflammatory response to irritation (*14*). Because respiratory fluids are rich in proteins, they help bacteria to proliferate and overwhelm the body's ability to expel the organisms, as is the case with pneumonia (*37*). Skin rashes and irritation of mucus membranes are also common adverse effects reported by people who say they have been exposed to sewage sludges. Like any break in the skin, rashes compromise the structural integrity of the outer layers of tissues and thereby provide a portal of entry for infectious microorganisms.

Methods used in processing sewage sludges should be reevaluated. Benefits from lime stabilization may be lost when increased susceptibility to respiratory infections develops from inhaling highly alkaline dusts. Similarly, the benefits of dewatering (thickening) sewage sludges with cationic polymers should be weighed against increased risks of infection caused by inhaling irritant organic amines from decomposed polymers.

***Ban Class B biosolids?*** Because the 503 Rule allows state and local governments to set stricter standards, a number of counties across the United States have banned land application of Class B biosolids after local citizens alleged adverse health effects. Unfortunately, if this trend continues, application of Class B sewage sludge will eventually be concentrated in areas where citizens lack the political and economic resources to deal with environmental problems.

However, public concerns associated with sewage sludges may not be resolved simply by banning Class B sludges. Exposure to chemical irritants increases our susceptibility to infections from all sources. Therefore, some level of concern is likely to remain regarding Class A sludges that cause respiratory problems and eye, nose, throat, and skin irritation. Once again, infection control problems associated with processed sewage sludges should be viewed in terms of pathogen–chemical risks.

Clearly, what is needed is a scientifically sound approach to land application practices with a broad base of public support. In the long run, a plan that includes restricting public exposure, reducing levels of chemical irritants, and moving to a Class A standard may ultimately be the best strategy to gaining acceptance within the scientific community and public domain.

## References


(1) U.S. Environmental Protection Agency. 40 Code of Federal Regulations, Part 503. *Fed. Regist. 58* (32), **1993,** 9248–9415.

(2) Renner, R. *Environ. Sci. Technol.* **2000,** *34*, 431A–435A.

(3) Lewis, D. L.; Gattie, D. K.; Novak, M. E.; Sanchez, S.; Pumphrey, C. *Sewage Sludge on Land: Public Health & Environmental Impacts*; Boston University School of Public Health. Boston, MA, Nov. 2, 2001 (www.bumc.bu.edu/www/sph/eh/sludgeConference).

(4) National Research Counsel. *Use of Reclaimed Water and Sludge in Food Crop Production*; Water Science and Technology Board, National Academy Press: Washington, DC, 1996.

(5) U.S. Department of Health and Human Services. Centers for Disease Control & Prevention, National Institute for Occupational Health & Safety. *Workers Exposed to Class B Biosolids During and After Field Application*. Publication No. 158, 2000, (www.cdc.gov/niosh).

(6) Environmental Criteria and Assessment Office. *Alternative Fuels Research Strategy*, Report EPA 600-AP-92/002, U. S. Environmental Protection Agency: Research Triangle Park, N. C., 1992.

(7) Lewis, D. L. *Nature* **1996,** *381*, 731–732.

(8) U.S. Environmental Protection Agency. *Biosolids Management and Enforcement Audit Report*; Report 2000-P-10; Office of Inspector General: Washington, DC, 2000.

(9) U.S. Environmental Protection Agency. *Land Application of Biosolids Status Report*. 2002-S-000004; Office of the Inspector General: Washington, DC, 2002.

(10) Berkow, R.; Fletcher, A. Infectious disease. In *The Merck Manual*, 16th ed.; Merck Research Laboratories: Rahway, NJ, 1992.

(11) Berkow, R.; Fletcher, A. Pediatrics and genetics. In *The Merck Manual*, 16th ed.; Merck Research Laboratories: Rahway, NJ, 1992.

(12) Berkow, R.; Fletcher, A. Diseases due to irritant gases and chemicals. In *The Merck Manual,* 16th ed., Merck Research Laboratories: Rahway, NJ, 1992.
(13) Schiffman, S. S. et al. *J. Agromed*. **2000,** *7*, 1–80.
(14) Norn, S.; Clementsen, P.; Kristensen, K. S.; Skov, P. S.; Bisgaard, H.; Gravensen, S. *Indoor Air* **1994,** *4*, 217–222.
(15) Lewis, D. L.; Garrison, A. W.; Wommack, K. E.; Whittemore, A.; Steudler, P.; Melillo, J. *Nature* **1999,** *401*, 898–901.
(16) Dowd, S. E; Gerba, C. P.; Pepper, I. L.; Pillai, S. D. *J. Environ. Qual.* **2000,** *29,* 343–348.
(17) Brook, I. *Int. J. Dermatol.* **1992,** *31,* 700–702.
(18) Leyden, J. J.; Kligman, A. M. *Arch. Dermatol.* **1978,** *114*, 56–59.
(19) U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Health and Safety (NIOSH). *Health Hazard Evaluation Report;* Report No. 98-0118-2748; NIOSH: LeSourdsville, OH, 1999.
(20) Dorn, R. C.; Reddy, C. S.; Lamphere, D. N.; Gaeuman, J. V.; Lanese, R. *Environ. Res.* **1985,** *38,* 332–359
(21) Brugha, R.; Heptonstall, J.; Farrington, P.; Andren, S.; Perry, K.; Parry, J. *Occup. Environ. Med.* **1998,** *55,* 567–569.
(22) Rylander, R. *Occup. Environ. Med.* **1999,** *56,* 354–357.
(23) Weldon, M.; VanEgdom, M. J.; Hendricks, K. A.; Regner, G.; Bell, B. P.; Sehulster, L. M. J. *Occup. Environ. Med.* **2000,** *42,* 83–87.
(24) Lewis, D. L. et al. M. *Lancet* **1992,** *340*, 1252–1254.
(25) Lewis, D. L.; Arens, M. *Nature Med.* **1995,** *1,* 956–958.
(26) Lewis, D. L.; Boe, R. K. *J. Clin. Microbiol.* **1992,** *30,* 401–406.
(27) U.S. Centers for Disease Control & Prevention. *Morbid. Mortal. Week. Rep.* **1993,** *42,* 1–12.
(28) U.S. Centers for Disease Control & Prevention. *Morbid. Mortal. Week. Rep.* **2001,** *50,* 941–948.
(29) Pasquill, F. *The Meteorol. Mag.* **1961,** *90,* 33–49.
(30) Lighthart, B.; Frisch, A. S. *Appl. Environ. Microbiol.* **1976,** *31*, 700–704.
(31) Parker, D. T.; Spendlove, J. C.; Bondurant, J. S.; Smith J. H. *J. Water Pollut. Control Fed.* **1977,** *49,* 2359–2365.
(32) Pillai, S. D.; Widmer, K. W.; Dowd, S. E.; Ricke, S. C. *Appl. Environ. Microbiol.* **1996,** *62*, 296–299.
(33) Lewis, D. L.; Gattie, D. K. *ASM News* **1990,** *56*, 263–268.
(34) Lewis, D. L.; Gattie, D. K. *ASM News* **1991,** *57*, 27–32.
(35) Influence of External Factors on Viability of Micro-organisms. In *Micro-organisms Function, Form and Environment;* Hawker, L. E.; Linton, A. H., Eds. University Park Press: Baltimore, MD, 1979.
(36) Lewis, D. L.; Gattie, D. K. *Ecol. Model.* **1991,** *55,* 27–46.
(37) Berkow, R.; Fletcher, A. Pulmonary disorders. In *The Merck Manual,* 16th ed.; Merck Research Laboratories: Rahway, NJ, 1992.

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